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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/539,382	03/31/2000	Alison A. McCormick	LSB-001/CIP	9680

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/539,382	MCCORMICK ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54,56,60-64,66,67,69,72,73 and 76-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54,56,60-64,66,67,69,72,73 and 77-86* is/are rejected.

7)☒ Claim(s) *76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed 4/4/2003 (paper no. 22) is acknowledged and entered into the record. Accordingly, claims 55, 57-59, 65, 68, 70-71, and 74-75 are canceled without prejudice or disclaimer, claims 77-86 are newly added.

2. Claims 54, 56, 60-64, 66-67, 69, 72-73, and 76-86 are pending and examined on the record.

New Arguments

Claim Rejections - 35 USC § 103

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 54,56,60-64,66-67,69,72-73, and 77-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caspar *et al* (previously cited) in view of Fiedler *et al* (Immunotechnology 1997 Oct; 3(3):205-216) and Ladner (US Patent 4704692). Claims are drawn to a polynucleotide encoding a polypeptide epitope of a B-cell lymphoma surface Ig antigen, wherein the polypeptide is encoded at least in part by a nucleic acid in the cell of the tumor and a nucleic acid sequence promoting expression of the polypeptide in a plant cell or plant, which polypeptide (1) includes an epitope unique to or overexpressed by tumor (2) is produced by a plant cell (3) is obtained fro the plant cell in correctly folded form (4) and is capable of inducing an immune response (claim 54); wherein the polypeptide is produced in a transiently in a plant (claim 56); wherein the polypeptide further comprises two V regions domains from Ig (claim 60), wherein the

two domains are at least in part Vh and Vl domains of an Ig (claim 61), wherein the Vh region includes at least one CDR (claim 62), wherein the CDR is CDR2 (claim 63), wherein said polypeptide is a two domain scFv (claim 64); wherein the polypeptide is linked by a linker that is (a) between 1 and 50 amino acid residues (b) consists of 1 and 12 different amino acids (c) facilitates secretion and correct folding of the polypeptide (claim 66), wherein the linker is a member of a randominzed library or linkers with the following requirements: position 1 cannot be the same nucleotide as position 2 of a repeated triplet, position 2 cannot be the same nucleotide as position 3 of a repeated triplet, and position 1 cannot be the same nucleotide as position 3 of a repeated triplet (claim 67), wherein the linker at position 1 is dA or dG, position 2 is dC or dG, and position 3 is dT (claim 69); wherein said immune response is a protective anti-tumor immune response (claim 72); wherein on administration a polyclonal anti-idiotypic antibody response or cell mediated immune response is induced (claim 73). The claims are also limited to a polynucleotide encoding a two domain scFv wherein the first domain and second domain is linked by a linker with the following properties: (i) has 1-50 amino acid residues (ii) consists of between 1 and 12 different amino acids (iii) facilitates secretion and correct folding of the polypeptide (iv) is a member of a randominzed library of linkers with the following requirements: position 1 cannot be the same nucleotide as position 2 of a repeated triplet, position 2 cannot be the same nucleotide as position 3 of a repeated triplet, and position 1 cannot be the same nucleotide as position 3 of a repeated triplet (claim 77), wherein the linker at position 1 is dA or dG, position 2 is dC or dG, and position 3 is dT (claim 78); wherein the scFv

includes at least in part the vh domain and Vl domain (claim 79), wherein the domains are those from a surface Ig epitope of a B-cell lymphoma (claim 80).

Caspar *et al* a polynucleotide sequence that encodes a scFv derived from a B-cell lymphoma Ig surface antigen. Because the scFv taught by Caspar *et al* is a scFv, it has two V-regions, one Vh and one Vl, wherein the Vh region (see figure 1 for example) includes at least one CDR of wherein it is a CDR2 (see page 3700) and is comprised of at least two domains. Furthemore, Caspar *et al* teaches that the scFv is linked together by a linker sequence. Moreover, Caspar *et al* teaches that although weak, the scFv administered did show an immune response (see page 3702 2nd column). Caspar *et al* does not specifically characterize the scFv as a molecule that can been produced by plant cells or a having a nucleic acid promoter sequence directing its production in a plant cell, nor does he specifically teach linkers with the criteria taught in the claimed limitations. Such deficiencies are remedied by Fiedler *et al* and Ladner.

Fiedler *et al* teach that scFv can be made in high quantities in transgenic plant cells, wherein 4-6% to 3-4% of the total protein found in leaves and seed, respectively, can be recombinantly expressed scFv. Furthermore, Fiedler *et al* teach that such recombinant scFv is functionally active.

Ladner taught that the conjugation of two proteins with a linker or two could produce a single chain polypeptide that was correctly folded and that the linker used was important so as to provide the correct amount of flexibility during the folding of the protein.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have a polynucleotide sequence encoding a protein comprising B-cell Ig epitopes wherein the protein has two domains, comprises a Vh and Vl domain conjugated together by a linker, and produced in a plant. One of skill in the art would have been motivated in doing so because Caspar *et al* taught the extraction and isolation of an antibody or Ig derived from a B-cell lymphoma and that the Vh and Vl domains of the surface Ig molecule could be linked together with a linker so as to create a scFv. The use of any linker in place of that taught by Caspar *et al* would be obvious because the function of the linker is to provide spacing between two or more functional domains so as to eliminate steric hindrance and to allow proper folding and flexibility during the folding process as taught by Ladner. Furthermore, because Fiedler *et al* taught that the scFv proteins could be made in plants and that plant production of recombinant proteins was high and produced active molecules, one of skill would have been motivated to use a plant system to produce functional and active proteins. Furthermore, Fiedler *et al* teach that plant could potentially provide long term storage for scFv produced. One of ordinary skill in the art would have expected a reasonable amount of success in making a polynucleotide such as the one claimed because both Fiedler *et al* and Ladner taught that modification to the production system of scFv and the linking of Vh and Vl domains with the appropriate linker to make a scFv were feasible and successful.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in Paper No. 22.

Conclusion

5. Claim 76 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 54,56,60-64,66-67,69,72-73, and 77-80 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
December 12, 2003

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600